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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,722	11/19/2001	Avi J. Ashkenazi	P2730P1C63	1427

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EXAMINER
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WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/989,722	ASHKENAZI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 119-126, 129-131 and 135-145 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 119-126, 129-131 and 135-145 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

**Detailed Action**

***Status of Application, Amendments, and/or Claims***

The Amendment, submitted 24 June 2004 has been entered. Claims 139-145 are added. Claims 119-126, 129, 130 and 135 are amended. Claims 127, 128 and 132-134 are cancelled.

Claims 119-126, 129-131 and 135-145 are under examination in the Instant Application.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

**Withdrawn Objections And/or Rejections**

***URL's***

The objection to the Specification because it contained browser-executable code, is *withdrawn*. Applicants amended the Specification to remove all URL's (23 June 2004).

***35 USC § 112, first paragraph – Deposit Rules***

The rejection of Claims 119-138 under 35 U.S.C. § 112, first paragraph, for not complying with the enablement requirement, is *withdrawn*. Applicants amended the Specification to insert language guaranteeing unrestricted availability of the deposited

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nucleic acid molecules (clone DNA59842-1502), and pointed out that the instant Specification lists the ATCC address.

***35 U.S.C. § 112, first paragraph-, Written Description.***

The rejection of Claims 124, 125 and 126 under 35 U.S.C. § 112, first paragraph, Written Description, is *withdrawn*. Applicants amended claims to remove language pertaining to functional regions of SEQ ID NO: 351 that have not been identified (i.e, "extracellular domains").

***35 USC § 102***

The rejection of Claim 134 under 35 U.S.C. 102(b) as being unpatentable over Davies, et al, 1996, (Accession No. HSU51280) is *withdrawn*. Applicants cancelled claim 134 in the paper of 23 June 2004.

***35 USC § 112, second paragraph***

The rejection of Claims 119-138 under 35 U.S.C. 112, second paragraph, for indefinite claim language, is *withdrawn*. Applicants amended current claims to remove phrases pertaining to a peptide "extracellular domain" and added language describing stringent hybridization conditions (23 June 2004).

**Maintained Objections and/or Rejections*****Continuity***

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119. Applicants have argued that they are entitled to the benefit of Provisional Application 60/141,037. However, since the claimed invention does not have Utility, the Provisional patent applications listed, although disclosing the same experimental assays as the instant specification, do not impart Utility to the instant invention. Therefore, the filing date of 19 November 2001 is considered as the priority date.

***35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.***

Claims 119-126, 129-131 and 135-145 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under 35 U.S.C. § 101 are set forth at pp. 3-11 of the previous Office Action (23 March 2004). Claims 119-126, 129-131 and 135-145 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (23 March 2004), one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue (23 June 2004, page 12) that the results presented in the instant Specification are enabling for the nucleic acid of SEQ ID NO: 350, encoding the polypeptide of SEQ ID NO: 351. They argue that the PRO1153 nucleic acid is a diagnostic marker for certain tumors, and point to the results of the amplification assay

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which showed an approximately 2-fold amplification of the PRO1153 DNA in adenocarcinomas and lung squamous cell carcinomas.

Applicant's arguments (23 June 2004) have been fully considered but are not found to be persuasive for the following reasons:

In the instant case, the specification provides data showing a very small increase in DNA copy number -1.5 to 2.5-fold- in two types of cancer. However, there is no evidence regarding whether or not PRO1153 mRNA or polypeptide levels are also increased in this cancer. Furthermore, as discussed in the previous Office Action (23 March 2004, page 13), what is often seen is a *lack* of correlation between DNA amplification and mRNA levels (Pennica, et al, 1998, Proc. Natl. Acad. Sci., 95: 14717-14722). As discussed by Haynes et al (1998, Electrophoresis, 19: 1862-1871), polypeptide levels cannot be accurately predicted from mRNA levels, and that, in their results the ratio varied from zero to 50-fold (page 1863). The literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). Applicants argue (23 June 2003, page 12) that the

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claims are directed to "nucleic acids [...]" and not to polypeptides or mRNA", and as such, protein and mRNA levels are not important in evaluating the disclosed PRO1153 nucleotide in terms of Utility. However, as discussed in the previous Office Action (23 March 2004), Utility of a novel nucleic acid presumably involved in cancer will depend in part on the role that the expressed polypeptide plays in cancer initiation, progression, growth, maintenance, etc. Furthermore, the PRO1153 *DNA* (gene) occurs in every cell. It is only where and when genes are expressed that we see critical differences between tissues. Finally, as discussed in the previous Office Action (23 March 2004), Hittleman, W., 2001, *Ann. NY. Acad. Sci.*, 952: 1-12), an increased in chromosome number is a common occurrence in cancerous cells and would result in a positive  $\Delta C_t$  measurement in the instant Specification.

Given how little the DNA copy number of PRO1153 increased, and the evidence provided by Haynes et al., Hittleman, W., Pennica et al and Hu, et al, it is clear that one skilled in the art would not assume that a small increase in gene copy number would correlate with significantly increased mRNA or polypeptide levels. Further research must be done to determine whether or not the PRO1153 polypeptide levels increased significantly in the tumor samples. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in *Brenner v. Manson*, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a

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process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,

"a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the Specification's assertions that the claimed PRO1153 polypeptides have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

***35 USC § 112, first paragraph – Written Description.***

Claims 119-123 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The reasons for this rejection under *35 U.S.C. § 112, first paragraph*, are set forth at pp. 9-11 of the previous Office Action (23 March 2004). Briefly, the Applicants were not in possession of all or a representative number of polynucleotides that have 80-99% homology to SEQ ID NO: 350 and still retain the function of SEQ ID NO: 350.

Applicants discuss the legal standards applied when evaluating Written Description, especially the requirement that the Specification must be evaluated by one of skill in the art (page 13, 23 June 2003). The examiner takes no issue with the discussion of general requirements for evaluating Written Description in this case. However, Applicants have not described or shown possession of all polynucleotides 80-99% homologous to SEQ ID NO: 350, that still retain the function of SEQ ID NO: 350. Nor



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have Applicants described a representative number of species that have 80-99% homology to SEQ ID NO: 350, such that it is clear that they were in possession of a genus of polynucleotides functionally similar to SEQ ID NO: 350.

As discussed in the previous Office Action (23 March 2003) even a very skilled artisan could not envision the detailed chemical structure of all or a significant number of encompassed PRO1153 polynucleotides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making or using the claimed polynucleic acids. The polynucleotide itself is required. Recitation of the phrase "wherein said nucleic acid is amplified in adenocarcinomas or squamous cell carcinomas of lung," (amended claims, 23 June 2003), is not adequate to describe the polynucleotides that have 80-99% homology to the PRO1153 polynucleotides, since there was no reduction to practice to support the amended claims. Applicants neither made nor tested variant polynucleotides, and as recited in the current Written Description Guidelines, Applicants must have invented the subject matter that is claimed and must be in "possession" of the claimed genus (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

### ***Conclusion***

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire Later than SIX MONTHS from the mailing date of this final action.

**Advisory information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW  
20 September 2004



ELIZABETH KEMMERER  
PRIMARY EXAMINER